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EXAMINER	
HARLE, JENNIFER I	

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Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER	
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Commissioner for Patents

Attached is a courtesy copy of the requested revised Election/Restriction requirement pusuant to the telephone interview. The time period will not be restarted pursuant to mutual agreement.

ATTACHMENT COURTESY COPY

DETAILED ACTION

1. Applicant's amendment, filed December 9, 2004, has been entered,

Claims 1-76 have been canceled

Claims 77-104 have been added.

Claims 77-104 are subject to an Election/Restriction Requirement.

2. The instant claims now encompass a myriad of inhibitors that are selective for a vast assortment of enzymes (both mutant and wild type), which as set forth reads on all known and unknown inhibitors and enzymes from a plethora of starting materials (see instant Specification, including Detailed paragraph [0077], [0078], [0131], [0132], [0133], [0143], [0137], [0138], [0139], [0140], [0143]-[0145], [0221]).

Therefore, the claims are drawn to patentably distinct products as they read on both the inhibitors and the targets of said inhibitors, wherein each inhibitor-target differs in structure and modes of action to such an extent and require non-coextensive searches to such an extent that they are considered separately patentable. For example, the claims encompass competitive, uncompetitive, and non-competitive inhibitors (e.g. see paragraph [0077], of the instant specification), a plethora of different enzymes with different structures and different actions, i.e. kinases and transferases and more specifically protein kinases and methyltransferases (e.g. see paragraphs [0063], [0064], [0068], [0070]), pyrazolopyimidine inhibitors and orthogonal ATP analogs and damnacanthal and CGP 57148 and additional inhibitors (see e.g. Figs. 9-12 paragraphs [0132], [0179]-[-[279]) .

The examiner notes that each of the inhibitors as well as each of the targets do not share a substantial structural feature essential to a common utility:

Not all possible orthogogonal N^6-ATP analogs are able to accepted as substrates by existing cellular kinase, i.e. some of them were not "dead subststrates", i.e. some were reactive (see e.g. [0186]-[0187].

Inhibitors may require that different position in the protein sequence of the kinase be modified to make an engineered kinase that will bind to them but such different modifications are well within the scope of the present invention (see e.g. Fig. 12, paragraph [0131]).

Each inhibitor is a patentable distinct invention for the following reasons. They are composed of chemical compounds, polypeptides, nucleotides, and derivatives/homologs of each these (see, e.g. (Figs. 2, 9-12, 14, [0071]-[0077], [0082], [0089], [0091], [0132], [0133], [0134]) and are structurally distinct molecules. Any relationship between the polynucleotide and the polypeptide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. One particular polynucleotide does not necessarily encode two different polypeptides. For example a nucleic acid, which hybridized one specific enzyme or inhibitor, even under stringent conditions, encompasses molecules, which contain point mutations, splice sites, frameshift mutations or stop codons which would result in us of a different open reading frame, and thus encode a protein that lacks any significant structure in common with a second inhibitor or enzyme. In addition, the inhibitor/enzymes can be made by methods using various methods not necessarily applicable to each other, i.e. chemical synthesis, peptide synthesis, recovery from natural sources using biochemical means, different types of extractions. For example, some of

the enzymes/inhibitors can be isolated using affinity chromatography and others can be made by straight chemical synthesis. Noting that these compounds are known and unknown, as set forth above. **For these reasons each inhibitor/enzyme is patentably distinct and applicant is required to select one inhibitor and one of each type of enzyme (wild type and mutant).**

Furthermore, searching all of the inhibitors and enzyme combinations together would impose a serious search burden. The search of the inhibitors and enzyme combinations is not coextensive. In cases such as this one, there is a serious search burden in the non-patent literature and structure searching may also be required. A search of one inhibitor/enzyme would not necessarily provide another inhibitor that has a different structure or sequence (if available). Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides, which would not have described the polynucleotide. Similarly there may have been "classical" genetics papers, which had no knowledge of the polypeptide but spoke of the gene or "classical" chemistry papers that spoke of the compound. Searching therefore is not co-extensive. This search requires an extensive analysis of the art retrieved and will require an in-depth analysis of technical literature. The scope of the inhibitors/enzymes claimed extend beyond mere chemical/polynucleotide/polypeptide compounds, as explained above. As such, it would be burdensome to search more than one inhibitor, one mutant enzyme and one wild type enzyme together.

Given the vast number of possibilities of patentably distinct inhibitors as they read on a vast number of patentably distinct enzymes/ targets, applicant is required to pick a specific inhibitor as it reads on a specific enzyme (e.g. inhibitor N^6-(cyclopentyloxy)ATP, 4-amino-1-

(tert-butyl)-3-(m-phenoxyphenyl)pyrazolo[3,4-d]pyrimidine – wild type enzyme – vScr, Cdc28; mutant type enzyme – V323A v-Src, Cdc28-as1).

At this time, it is extremely difficult for the examiner to ascertain the number of possibilities of patentably distinct Inventions, given the broad scope of the claimed inventions and disclosure of numerous possibilities of known and unknown inhibitors and targets disclosed in the specification as filed.

Therefore, the examiner has not set forth discrete Groups at this time.

3. According to the specification (see, e.g. paragraph [0018]), the present invention provides a strategy of combining chemical and genetic approaches to enable the rapid generation of highly selective small molecule inhibitors for engineered enzymes.

However, it is unclear at this time whether Applicants' application provides sufficient written description and enablement under 35 U.S.C. , first paragraph, for the specific inhibitors currently claimed or whether the claimed inhibitors are the result of identifying said inhibitors via screening assays ,e.g. reach through claims. As pointed out above, it is extremely difficult for the examiner to ascertain the structure(s) of the claimed inhibitors as well as any correlation between structure and function of the claimed inhibitors.

4. In the interest of compact prosecution, Applicants are invited to provide claims that distinctly recite Applicants invention(s) as they read on a specific inhibitor as it reads on a particular target enzyme.

Alternatively, should Applicants traverse on the ground that each of the inhibitors and its corresponding target enzyme are not patentably distinct, Applicants should submit evidence or identify such evidence now of record showing that the inhibitors and target enzymes are obvious

variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the invention.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. A first set of Groups is drawn to the inhibitors selective for an enzyme.

II. A second set of Groups is the method of inhibiting a catalytic activity of a mutant enzyme by contact the mutant enzyme with an inhibitor with selectivity for an enzyme.

III. A third set of Groups is the method of inhibiting the growth of a cell that expresses a mutant enzyme by contacting the cell with an inhibitor with selectivity for an enzyme.

IV. A fourth set of Groups is the method of disrupting transformation in a cell that expresses a mutant enzyme comprising contacting a cell with an inhibitor with selectivity for an enzyme.

V. A fifth set of Groups is the method of inhibiting phosphorylation of a substrate of a mutant enzyme by incubating an inhibitor with selectivity for an enzyme with a mixture of the mutant enzyme and its substrate.

The first set of Groups and the second through fifth set of Groups are related as product and process of use. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the inhibitors can be used in assays or purifications.

Searching the first set of Groups and the second through fifth set of Groups would impose serious search burden. In the instant case, the search for the inhibitors/enzymes and the methods using the inhibitors are not co-extensive. The first set of Groups encompasses a plethora of compounds both discloses and undisclosed that vary completely in terms of structure and method of search, which are not required for the second through fifth set of groups. In contrast, the search for the second through fifth groups would require a text search for the various methods in addition to the structure, registry, sequence, homology, ect. Search. Prior art searches that teach the specific inhibitors/enzymes would not necessarily be applicable to the different methods of using them. Moreover, even if the inhibitors/enzymes were known, the methods of using them may be novel and unobvious in view of the preamble or active steps.

The second through fifth set of Groups are subcombinations capable of use together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, each group has a separate utility, the second Group is separately usable because it is carried outside of a cell and encompasses a plethora of activites, i.e. more than just phosphorylation – interaction with transferase, polymerase, hyrolase, etc.; while the third Group works within a cell and inhibits the Growth of a living cell; the fourth Group also acts within a living cell and disrupts transformation in a cell that expresses a mutant enzyme but does not necessarily inhibit growth if it operates on a different pathway; and the fifth Group is carried on outside a cell and only encompasses phosphorylation and must include incubation. Thus, they are all separately usable because they utilize different mechanisms of action and could use different inhibitors/enzymes and operate under different conditions (group. See MPEP § 806.05(d).

Furthermore, searching the second through fifth set of Groups would impose a serious search burden. In the instant case, the search for the different methods of use is not co-extensive. They have different method steps, require different search strategies and encompass different key concepts to be incorporated into the search. As such, it would be burdensome to search the second through fifth set of groups together.

If any of the Groups are selected Applicant must also select a specific inhibitor/enzyme, i.e. select one inhibitor and one of each type of enzyme (wild type and mutant), given the vast number of possibilities of patentably distinct inhibitors as they read on a vast number of patentably distinct enzymes/ targets, applicant is required to pick a specific inhibitor as it reads on a specific enzyme (e.g. inhibitor N^6-(cyclopentyloxy)ATP, 4-amino-1-(tert-butyl)-3-(m-phenoxyphenyl)pyrazolo[3,4-d]pyrimidine – wild type enzyme – vScr, Cdc28; mutant type enzyme – V323A v-Src, Cdc28-as1), as they are each patentably distinct and burdensome in and of themselves for the reasons set forth above.

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP §821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to the final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirement of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in Light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claim or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, not that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

6. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143). Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer I. Harle whose telephone number is (571) 272-2763. The examiner can normally be reached on Monday through Thursday, 6:30 am to 5:00 pm,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S/

Jennifer I. Harle
Examiner
Art Unit 1654

April 15, 2005